TRAVASOL - leucine, phenylalanine, lysine hydrochloride, methionine, isoleucine, valine, histidine, threonine, tryptophan, alanine, glycine, arginine, proline and tyrosine injection
Baxter Healthcare Corporation

DESCRIPTION

5.5% and 8.5% Travasol® (Amino Acid) Injections are sterile, nonpyrogenic, hypertonic solutions of essential and nonessential amino acids provided in a Pharmacy Bulk Package. A Pharmacy Bulk Package is a container of a sterile preparation for parenteral use that contains many single doses. The contents are intended for use in a pharmacy admixture program and are restricted to the preparation of admixtures for intravenous infusion.

The Viaflex® plastic container is fabricated from a specially formulated polyvinyl chloride (PL 146® Plastic). Exposure to temperatures above 25°C/77°F during transport and storage will lead to minor losses in moisture content. Higher temperatures lead to greater losses. It is unlikely that these minor losses will lead to clinically significant changes within the expiration period. The amount of water that can permeate from inside the container into the overwrap is insufficient to affect the solution significantly. Solutions in contact with the plastic container can leach out certain of its chemical components in very small amounts within the expiration period, e.g., di-2-ethylhexyl phthalate (DEHP), up to 5 parts per million; however, the safety of the plastic has been confirmed in tests in animals according to USP biological test for plastic containers as well as by tissue culture toxicity studies.

Each 100 mL of 5.5% and 8.5% Travasol® (Amino Acid) Injection contains:

	5.5%	**8.5%**
Amino Acids	5.5 g	8.5 g
Total Nitrogen	925 mg	1.43 g
pH	6.0 (5.0 to 7.0)	6.0 (5.0 to 7.0)

(pH adjusted with glacial acetic acid and may have been adjusted with sodium hydroxide)

Essential Amino Acids		
Leucine – $C_6H_{13}NO_2$	340 mg	526 mg
Phenylalanine – $C_9H_{11}NO_2$	340 mg	526 mg
Lysine (added as the hydrochloride salt) – $C_6H_{14}N_2O_2$	318 mg	492 mg
Methionine – $C_5H_{11}NO_2S$	318 mg	492 mg
Isoleucine – $C_6H_{13}NO_2$	263 mg	406 mg
Valine – $C_5H_{11}NO_2$	252 mg	390 mg
Histidine – $C_6H_9N_3O_2$	241 mg	372 mg
Threonine – $C_4H_9NO_3$	230 mg	356 mg
Tryptophan – $C_{11}H_{12}N_2O_2$	99 mg	152 mg
Nonessential Amino Acids		
Alanine – $C_3H_7NO_2$	1.14 g	1.76 g
Glycine – $C_2H_5NO_2$	1.14 g	1.76 g
Arginine – $C_6H_{14}N_4O_2$	570 mg	880 mg
Proline – $C_5H_9NO_2$	230 mg	356 mg
Tyrosine – $C_9H_{11}NO_3$	22 mg	34 mg
Anion profiles per liter*		
Acetate†	43 mEq	67 mEq
Chloride‡	22 mEq	34 mEq
Osmolarity (Calc.)	569 mOsmol/L	880 mOsmol/L

*****Balanced by ions from amino acids.
†derived from pH adjustment with glacial acetic acid.
‡contributed by the lysine hydrochloride.

CLINICAL PHARMACOLOGY

5.5% and 8.5% Travasol® (Amino Acid) Injections administered via central vein provide biologically utilizable source material for protein synthesis when used with concentrated calorie sources (such as hypertonic dextrose or fat emulsion), electrolytes, vitamins

and minerals. Administered peripherally after appropriate dilution or with minimal calorie supplementation (such as 5% dextrose), it enhances the conservation of body protein.

INDICATIONS AND USAGE

5.5% and 8.5% Travasol® (Amino Acid) Injections are indicated as an adjunct in the offsetting of nitrogen loss or in the treatment of negative nitrogen balance in patients where: (1) the alimentary tract cannot or should not be used, (2) gastrointestinal absorption of protein is impaired, or (3) metabolic requirements for protein are substantially increased, as with extensive burns.

Central Vein Administration:
Central vein infusion should be considered when amino acid solutions are to be admixed with hypertonic dextrose to promote protein synthesis such as for hypercatabolic or depleted patients or those requiring long term parenteral nutrition.

Peripheral Vein Administration:
For patients in whom the central vein route is not indicated, amino acid solutions diluted with low dextrose concentrations may be infused by peripheral vein when supplemented with or without added fat emulsion.

Protein-Sparing:
Dilute amino acid solutions for **peripheral administration** may be used in patients who exhibit no clinically significant protein malnutrition. The purpose of the solution is to replace protein losses which occur in relation to an intercurrent phenomenon which is known or suspected to be productive of a protein loss condition for a short or moderate period of time. Protein-sparing can be achieved by peripheral infusion of amino acid solutions with or without dextrose.

CONTRAINDICATIONS

Hypersensitivity to one or more amino acids.
Severe liver disease or hepatic coma.
Anuria.

WARNINGS

These injections are for compounding only, not for direct infusion.

Caution should be exercised when admixing 5.5% and 8.5% Travasol® (Amino Acid) Injections. Studies have shown that admixtures of Travasol® (Amino Acid) Injection, 10% and 20% Travamulsion® Intravenous Fat Emulsion Injection and high concentration dextrose injection (10 to 70%) from Baxter Healthcare Corporation, are stable over short periods of time. These solutions should be used promptly after admixing. Any storage should be under refrigeration and limited to a brief period of time, preferably less than 24 hours. Reference should be made to Travamulsion® Injection and high concentration dextrose injection from Baxter Healthcare Corporation package inserts for detailed information on each component.
Proper administration of these injections requires a knowledge of fluid and electrolyte balance and nutrition as well as clinical expertise in recognition and treatment of the complications which may occur.
Administration of amino acid solutions to a patient with hepatic insufficiency may result in serum amino acid imbalances, hyperammonemia, stupor and coma.
Hyperammonemia is of **special significance in infants.** This reaction appears to be related to a deficiency of the urea cycle amino acids of genetic or product origin. It is essential that blood ammonia be measured frequently in infants.
Conservative doses of these injections should be given to patients with known or suspected hepatic dysfunction. Should symptoms of hyperammonemia develop, administration should be discontinued and the patient's clinical status reevaluated.
Administration of amino acid solutions in the presence of impaired renal function presents special issues associated with retention of electrolytes.
These injections should not be administered simultaneously with blood through the same infusion set because of the possibility of pseudoagglutination.
WARNING: This product contains aluminum that may be toxic. Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired. Premature neonates are particularly at risk because their kidneys are immature, and they require large amounts of calcium and phosphate solutions, which contain aluminum.
Research indicates that patients with impaired kidney function, including premature neonates, who receive parenteral levels of aluminum at greater than 4 to 5 μg/kg/day accumulate aluminum at levels associated with central nervous system and bone toxicity. Tissue loading may occur at even lower rates of administration.
Administration by central venous catheter should be used only by those familiar with this technique and its complications.

PRECAUTIONS

It is essential to provide adequate calories concurrently if parenterally administered amino acids are to be retained by the body and utilized for protein synthesis. Concentrated dextrose solutions are an effective source of such calories.

With the administration of 5.5% and 8.5% Travasol® (Amino Acid) Injections in combination with highly concentrated dextrose solutions, hyperglycemia, glycosuria and hyperosmolar syndrome may result. Blood and urine glucose should be monitored on a routine basis in patients receiving this therapy.
Sudden cessation in administration of a concentrated dextrose solution may result in insulin reaction due to continued endogenous insulin production. Parenteral nutrition mixtures should be withdrawn slowly.
Electrolytes may be added to these injections as dictated by the patient's electrolyte profile.
The metabolizable acetate anion and amino acid profiles in these injections were designed to minimize or prevent occurrences of hyperchloremic metabolic acidosis and hyperammonemia. However, the physician should be aware of appropriate countermeasures if they become necessary.
Strongly hypertonic nutrient solutions should be administered through an indwelling intravenous catheter with the tip located in the superior vena cava.
Because of its antianabolic activity, concurrent administration of tetracycline may reduce the protein-sparing effect of infused amino acids.
Care should be taken to avoid excess fluid accumulation, particularly in patients with renal disease, pulmonary insufficiency and heart disease.
During protein-sparing therapy in the absence of supporting carbohydrate metabolism, an accumulation of ketone bodies in the blood often occurs. Correction of ketonemia usually can be accomplished by administering some carbohydrates.
Protein-sparing therapy is useful for periods up to 10 to 12 days. Patients requiring nutritional support thereafter should be placed on oral or parenteral regimens that employ adequate nonprotein calorie components.
Drug product contains no more than 25 µg/L of aluminum.

Laboratory Tests
Frequent clinical evaluation and laboratory determinations are necessary for proper monitoring during administration. Studies should include blood sugar, serum proteins, kidney and liver function tests, electrolytes, hemogram, carbon dioxide combining power or content, serum osmolarities, blood cultures and blood ammonia levels.

Carcinogenesis and Mutagenesis and Impairment of Fertility

Studies with 5.5% and 8.5% Travasol® (Amino Acid) Injections have not been performed to evaluate carcinogenesis potential, mutagenic potential, or effects on fertility.

Pregnancy

Teratogenic Effects

Pregnancy Category C.

Animal reproduction studies have not been conducted with 5.5% and 8.5% Travasol® (Amino Acid) injections. It is also not known whether 5.5% and 8.5% Travasol® (Amino Acid) Injections can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. 5.5% and 8.5% Travasol® (Amino Acid) Injections should be given to a pregnant woman only if clearly needed.

Do not use unless solution is clear and seal is intact.

Nursing Mothers

Caution should be exercised when 5.5% and 8.5% Travasol® (Amino Acid) Injections are administered to a nursing woman.

Pediatric Use

Safety and effectiveness of 5.5% and 8.5% Travasol® (Amino Acid) Injections in pediatric patients have not been established by adequate and well-controlled studies. However, the use of amino acid injections in pediatric patients as an adjunct in the offsetting of nitrogen loss or in the treatment of negative nitrogen balance is referenced in the medical literature. SeeDOSAGE AND ADMINISTRATION.

SPECIAL PRECAUTIONS
Administration of amino acid solutions and other nutrients via central or peripheral venous catheter may be associated with complications which can be prevented or minimized by careful attention to all aspects of the procedure. This includes attention to solution preparation, administration and patient monitoring. **It is essential that a carefully prepared protocol, based on current medical practices, be followed, preferably by an experienced team.** Although a detailed discussion of the complications is beyond the scope of this insert, the following summary lists those based on current literature:

Technical:
The placement of a central venous catheter should be regarded as a surgical procedure. The physician should be fully acquainted with various techniques of catheter insertion as well as recognition and treatment of complications. For details of techniques and placement sites consult the medical literature. X-ray is the best means of verifying catheter placement. Complications known to occur from the placement of central venous catheters are pneumothorax, hemothorax, hydrothorax, artery puncture and transection, injury to the brachial plexus, malposition of the catheter, formation of arteriovenous fistula, phlebitis, thrombosis, cardiac arrhythmia and catheter embolus.

Septic:
The constant risk of sepsis is present during administration of parenteral nutrition solution. Since contaminated solutions and infusion catheters are potential sources of infection, it is imperative that the preparation of the solution and the placement and care of catheters be accomplished under controlled aseptic conditions. If fever develops, the solution, itsdelivery system and the site of the indwelling catheter should be changed.
Solutions ideally should be prepared in the hospital pharmacy under a laminar flow hood. The key factor in their preparation is careful aseptic technique to avoid inadvertent touch contamination during mixing of solutions and addition of other nutrients.

Metabolic:
The following metabolic complications have been reported: metabolic acidosis, hypophosphatemia, alkalosis, hyperglycemia and glycosuria, osmotic diuresis and dehydration, rebound hypoglycemia, elevated liver enzymes, hypo and hypervitaminosis, electrolyte imbalances and hyperammonemia. Frequent clinical evaluation and laboratory determinations are necessary, especially during the first few days of therapy, to prevent or minimize these complications.

ADVERSE REACTIONS
See WARNINGS and SPECIAL PRECAUTIONS.
Infusion of any hypertonic solution can result in local inflammatory reactions. Policies and procedures should be established for the recognition and management of such reactions.

OVERDOSAGE
See CONTRAINDICATIONS and WARNINGS.

DOSAGE AND ADMINISTRATION
If a patient is unable to take enteral nourishment for a prolonged period of time, institution of total parenteral nutrition (TPN) with exogenous calories should be considered.

The total daily dose of 5.5% and 8.5% Travasol® (Amino Acid) Injections depends on the patient's metabolic requirement and clinical response. The determination of nitrogen balance and accurate daily body weights, corrected for fluid balance, are probably the best means of assessing individual nitrogen requirements.
Recommended Dietary Allowances* of protein range from approximately 0.75 g/kg of body weight for adults to 1.68 g/kg for infants. It must be recognized, however, that protein as well as caloric requirements in traumatized or malnourished patients may be increased substantially. Daily amino acid doses of approximately 1.0 to 1.5 g/kg of body weight for adults with adequate calories are generally sufficient to satisfy protein needs and promote positive nitrogen balance.
For the initial treatment of trauma or protein calorie malnutrition, higher doses of protein with corresponding quantities of carbohydrate will be necessary to promote adequate patient response to therapy. The severity of the illness being treated is the primary consideration in determining proper dose level. Such higher doses, especially in infants, must be accompanied by more frequent laboratory evaluation.
For protein-sparing in well nourished patients not receiving significant additional calories, amino acid dosages of 1.0 to 1.7 g/kg/day reduce nitrogen losses and spare body protein. If daily increases in BUN in the range of 10 to 15 mg% for more than three days should occur, then protein-sparing therapy should be discontinued and a regimen with full nonprotein calorie substrates should be adopted.
Care should be exercised to insure the maintenance of proper levels of serum potassium. Quantities of 60 to 180 mEq of potassium per day have been used with adequate clinical effect. It may be necessary to add quantities of this electrolyte to these injections, depending primarily on the amount of carbohydrate administered to and metabolized by the patient.
Patients receiving these injections should be monitored (carefully) and their electrolyte requirements individualized.
Total daily fluid requirements can be met beyond the volume of amino acids solution by supplementing with noncarbohydrate or carbohydrate-containing electrolyte solutions.
Maintenance vitamins, additional electrolytes and trace elements should be administered as required.
Fat emulsion coadministration should be considered when prolonged parenteral nutrition (more than 5 days) is required in order to prevent essential fatty acid deficiency (EFAD). Serum lipids should be monitored for evidence of EFAD in patients maintained on fat free total parenteral nutrition.

Pediatric Use:

Use of 5.5% and 8.5% Travasol® (Amino Acid) Injections in pediatric patients is governed by the same considerations that affect the use of any amino acid solution in pediatrics. The amount administered is dosed on the basis of grams of amino acids/kg of body weight/day. Two to three g/kg of body weight for infants with adequate calories are generally sufficient to satisfy protein needs and promote positive nitrogen balance. Solutions administered by peripheral vein should not exceed twice normal serum osmolarity (718 m0smol/L).

Central Vein Administration:

Hypertonic mixtures of amino acids and dextrose may be administered safely by continuous infusion through a central vein catheter with the tip located in the vena cava. In addition to meeting nitrogen needs, the administration rate is governed, especially during the first few days of therapy, by the patient's tolerance to dextrose. Daily intake of amino acids and dextrose should be increased gradually to the maximum required dose as indicated by frequent determinations of urine and blood sugar levels.

In many patients, provision of adequate calories in the form of hypertonic dextrose may require the administration of exogenous insulin to prevent hyperglycemia and glycosuria.

Parenteral nutrition may be started with infusates containing lower concentrations of dextrose; dextrose content may be gradually increased to estimated caloric needs as the patient's glucose tolerance increases.

Sudden cessation in administration of a concentrated dextrose solution may result in insulin reaction due to continued endogenous insulin production. Such solutions should be withdrawn slowly.

Peripheral Vein Administration:

For patients requiring parenteral nutrition in whom the central vein route is not indicated, these injections can be mixed with low concentration dextrose solutions and administered by peripheral vein in conjunction with or without fat emulsions. In pediatric patients, the final solution should not exceed twice normal serum osmolarity (718 m0smol/L).

Intravenous fat emulsion provides approximately 1.1 kcal/mL (10%) or 2.0 kcal/mL (20%) and may be administered along with amino acid-dextrose solutions by means of a short Y-connector near the infusion site to supplement caloric intake. Fat, however, should not be the sole caloric intake since studies have indicated that glucose is more nitrogen sparing in the stressed patient.

Protein-Sparing:

For well nourished patients who require short-term parenteral support, these injections can be administered peripherally with or without carbohydrate calories. Such infusates can be prepared by dilution of these injections with Sterile Water for injection or 5% Dextrose Injection to prepare isotonic or slightly hypertonic solutions which may be administered by peripheral vein.

Depending upon the clinical condition of the patient, approximately 3 liters of solution may be administered per 24 hour period. When used postoperatively, the therapy should begin with 1000 mL the first postoperative day. Thereafter, the dose may be increased to 3000 mL per day.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. Use of a final filter is recommended during administration of all parenteral solutions, where possible, A slight yellow color does not alter the quality and efficacy of the product.

5.5% and 8.5% Travasol® (Amino Acid) Injection in the Pharmacy Bulk Package is intended for use in the preparation of sterile, intravenous admixtures. Additives may be incompatible with the fluid withdrawn from this container. Complete information is not available. Those additives known to be incompatible should not be used. Consult with pharmacist, if available. When compounding admixtures, use aseptic technique. Mix thoroughly. Do not store any unused portion of 5.5% and 8.5% Travasol® (Amino Acid) Injection.

Solutions should be used promptly after mixing. Any storage should be under refrigeration and limited to a brief period of time, preferably less than 24 hours.

DIRECTIONS FOR USE OF VIAFLEX® PLASTIC PHARMACY BULK PACKAGE CONTAINER

To Open

Tear overpouch down side at slit and remove solution container. Some opacity of the plastic due to moisture absorption during the sterilization process may be observed. This is normal and does not affect the solution quality or safety. The opacity will diminish gradually. Check for minute leaks by squeezing inner bag firmly. If leaks are found, discard solution as sterility may be impaired. For compounding only, not for direct infusion.

Preparation for Admixing

1. The Pharmacy Bulk Package is to be used only in a suitable work area such as a laminar flow hood (or an equivalent clean air compounding area).
2. Suspend container from eyelet support.
3. Remove plastic protector from outlet port at bottom of container.
4. Attach solution transfer set. Refer to complete directions accompanying set.

Note: The closure shall be penetrated only one time with a suitable sterile transfer device or dispensing set which allows measured dispensing of the contents.

5. Viaflex® containers should not be written on directly since ink migration has not been investigated. Affix accompanying label for date and time of entry.

6. Once container closure has been penetrated, withdrawal of contents should be completed without delay. After initial entry, maintain contents at room temperature (25°C/77°F) and dispense within 4 hours.

HOW SUPPLIED

5.5% and 8.5% Travasol® (Amino Acid) Injections are supplied in Viaflex® plastic Pharmacy Bulk Package containers in the following sizes and concentrations:

	500 mL	**1000 mL**
5.5%	2B6603 NDC 0338-0624-03	
8.5%	2B6613 NDC 0338-0626-03	2B6614 NDC 0338-0626-04

Exposure of pharmaceutical products to heat should be minimized. Avoid excessive heat. Protect from freezing. It is recommended the product be stored at room temperature (25°C/77°F). Protect from light until immediately prior to use.

Do not remove container from overpouch until ready to use.

Do not use if overpouch has been previously opened or damaged.

*Food and Nutrition Board National Academy of Sciences - National Research Council (Revised 1989)

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